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[54] **METHOD FOR PRODUCING INFLUENZA HEMAGGLUTININ MULTIVALENT VACCINES USING BACULOVIRUS**

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[57] **ABSTRACT**

A method of preparing a recombinant influenza vaccine using DNA technology is provided. The resulting vaccine is a trivalent influenza vaccine based on a mixture of recombinant hemagglutinin antigens cloned from influenza viruses having epidemic potential. The recombinant hemagglutinin antigens are full length, uncleaved (HA0), glycoproteins produced from baculovirus expression vectors in cultured insect cells and purified under non-denaturing conditions. The process for cloning influenza hemagglutinin genes from influenza A and B viruses uses specially designed oligonucleotide probes and PCR. The cloned HA genes are then modified by deletion of the natural hydrophobic signal peptide sequences and replacing them with a new baculovirus signal peptide. A general approach for the efficient extraction and purification of recombinant HA protein produced in insect cells is also disclosed which can be adapted for the purification of rHA proteins from A sub-types and B type influenza viruses. The procedure produces substantially pure rHA which is a biologically active hemagglutinin, non-denatured, and suitable as a component in human or other animal influenza vaccines.

11 Claims, 3 Drawing Sheets